Blending & Compressing

Group-A and group-B granules are uniformly blended by geometric dilution in a Paterson-Kelly (PK) twin shell blender. After discharge, the active component blend is serially mixed with the blend composition of group-A and group-B components for about 6-8 minutes. The final composition is discharged and compressed into a suitable sized compact.

Coating

If desired, the compressed compact may be coated with an aqueous or solvent based polymer solution. The choice of polymer, solvent and plasticizer may vary as required and it is dependent on the desired outcome. The polymer may be a functional coating such as a pH-dependent enteric polymer or a non-functional coating such as a hydrosoluble polymer for esthetics.

Example 2:

Two drug delivery systems were prepared in order to compare the kinetics of drug release and changes in dynamic volume profile of the delivery system (tablet). The control comprised a prior art formulation, (Prior Art, Table 1) and the second delivery system comprised the hydrostatic couple (components listed in Table 1) as prepared using the method of Example 1. The agent of interest in both delivery systems was caffeine.

Table 1: Components of Prior art and hydrostatic couple formulations

Component	Component	Amount per tablet (mg)
Prior art		
Active agent	Caffeine Anhydrous USP	160
Control Release polymer	Carbopol 971P USP/NF	224
Flow Promoter	Colloidal Silicon Dioxide	12
Lubricant	Magnesium Stearate	4

Hydrostatic couple		
Active agent	Caffeine Anhydrous USP	70
Hydrostatic couple		
Group-A	Carbopol 971P	280
Group-B	Crospovidone XL-10	8
Flow promoter	Colloidal Silicon Dioxide	4.3
Lubricant	Magnesium Sterate	3.67

The prepared delivery systems were placed within PBS at ~~pH7.0~~ pH 7.0 in a Type II USP 24 Dissolution apparatus at 37°C (±0.5) using a paddle speed of 50 rpm. Caffeine release from the delivery systems were measured over time. Caffeine release was determined spectrophotometrically @ 272nm.

Method for Measuring Dynamic Volume Change due to Fluid Imbibition

The dynamic volume change of a fluid-imbibing or swelling tablet was measured by computation of the density of the swollen tablet and its mass. The basic relationship is:

$$Vt=Mt/D$$

Where Vt is the volume at a given time; Mt, is the mass of swollen tablet at a given time; and D, is the density of the swollen tablet

To obtain dynamic volume values, the same tablet undergoing swelling in the fluid media was removed from the dissolution media at regular (pre-fixed) time intervals, weighed in air (to obtain its mass) and weighed submerged in the fluid media (to obtain its buoyancy). The tablet is immediately returned to the dissolution media where swelling resumes. The time lapse between removal from the fluid media and its return to the media is kept constant and short in order to minimize errors due to excessive dehydration. This time interval is typically not more than 30 seconds.

The density of the swollen tablet is obtained by calculating:

$$\rho 2=(A/P)*\rho o$$

where, ρ2 is the density of the swollen tablet; ρo is the density of the fluid media.

Equipment & Materials for Dynamic Volume Measurement

Swelling & Drug Dissolution Measurements

USP Dissolution Apparatus Type II (Paddle)

Settings: Rotational Speed: 40 – 50 rpm

Temperature: 37° C +/- 0.5°C

PBS buffer pH 7.00 (or suitable buffer at a desired pH).

Dynamic Volume Measurements

Mettler-Toledo Density Determination Kit (for liquids and Solids) Model # 33360

Media: PBS buffer pH 7.00 or suitable buffer at a desired pH.

Figure 1 shows a plot of the dynamic volume profile of a prior art formulation, demonstrating a linear volume increase associated with a hydrodynamic polymer (Group-A component). The corresponding drug release (dissolution profile) for this formulation is shown in Fig 3. A rapid release (exponential) of an agent of interest from the prior art delivery system, reaching a maximum release rate after about 3.5 to 4 hours is evident in Figure 3. This is the typical Fickian release manifested by prior art compositions using group A- type components as the control release polymer. With this delivery system, the rate of efflux of an agent of interest is due to passive diffusion and is substantially less than the rate of influx of the fluid. Consequently, the rate of release of an agent of interest is dependant on the chemical potential and concentration of the agent.

The dynamic fluid profile of a delivery system of the present invention comprising a hydrostatic couple provided in Table 1 is presented in Figure 2. Following an initial increase in the dynamic volume of the tablet, the volume remains stable over